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Levetiracetam for benign epilepsy of childhood with centrotemporal spikes—three cases

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Benign epilepsy with centrotemporal spikes (BECTS), also known as benign rolandic epilepsy (BRE) of childhood represents 15% of all childhood epilepsies [Handbook of Epilepsy Treatment (2000)]. A majority of these patients do no require treatment; however, in those cases where treatment is justified, the most efficacious medication with a benign safety profile should be selected. We present three clinical cases of otherwise healthy children with BECTS who were treated only with levetiracetam. All three of these children remain seizure-free and are experiencing no reported side effects.
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Key words: levetiracetam/keppra; seizure; children; benign epilepsy of childhood (benign rolandic); centrotemporal spikes.

INTRODUCTION

Benign epilepsy of childhood with centrotemporal spikes (BECTS), also known as benign rolandic epilepsy (BRE) is an epilepsy syndrome beginning at age 3–12 years in otherwise normal children. It represents 15% of all childhood epilepsies[1]. Most seizures affect the face and oropharyngeal muscles, but children may also experience convulsions. The electroencephalogram (EEG) may be normal, but typically reveals large epileptic spikes in the rolandic region. Treatment with antiepileptic drugs (AEDs) is not always required because seizures are infrequent, tend to occur during sleep, and the syndrome remits by age 16. However, factors in favour of treatment include a young age of onset, a short interval between the first three seizures, generalised convulsive seizures, and daytime seizures[2].

One major argument against AED treatment in this population is the disadvantage of medication side effects. Children who require treatment traditionally receive carbamazepine or valproic acid[3]. Gabapentin, a traditionally safer medication, suggested superiority over placebo in a recent double-blind, randomised, placebo-controlled trial, but the intent to treat analysis did not reach statistical significance ($P = 0.085$)[4]. Lamotrigine has also been reported for use in BECTS. In a retrospective study ($n = 4$) all of the children remained asymptomatic; however, the follow-up was less than 6 months[5].

However, seizures can warrant treatment when frightening and distressing to child or parents. Additionally, whether intellectual deterioration results from partial seizures remains unclear[6] and tonic clonic seizures expose the child to injury and may increase the risk of sudden unexpected death in epilepsy (SUDEP)[7].

Potential advantages of levetiracetam for the paediatric population include this novel drug's lack of non-linear elimination kinetics, autoinduction kinetics, drug–drug interactions, significant protein binding (<10%), or reactive metabolites such as epoxides, -enes, or oxides[8]. Levetiracetam does not cause the weight gain and thinning of hair seen with valproic acid, nor is it extensively metabolised in the liver[9]. Carbamazepine has a risk of rash of 10%[10], while the risk of rash with levetiracetam approximates placebo[11]. Levetiracetam also takes a relatively short time to achieve therapeutic dose, unlike lamotrigine which can take 5–6 weeks; and lamotrigine has a 6% chance of rash[5].

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CASE 1

SG presented 18 December 2000, at age 4 years 6 months with two episodes of right arm partial seizures lasting approximately 20 seconds. The first occurred while eating; her right arm shook and she suddenly fell backwards. She did not lose consciousness, but complained of a headache. Emergency room evaluation was unremarkable. The next day, during a nap at school, she had abnormal movements of her right arm. When she awoke, she was unable to move the right arm for about 10 minutes.

The patient was a 6 lb 7 oz product of a 40-week gestation, born via Caesarean section because of pre-eclampsia. Developmental milestones were normal. Apart from multiple ear infections, she has no significant past medical history. Family history was remarkable for childhood seizures in a maternal cousin. In addition, a great grandmother had grand mal seizures.

Physical and neurological examinations were normal. EEG revealed abundant focal spike discharges from the left centrotemporal region while awake. The brain MRI was normal. The patient began levetiracetam 250 mg each evening. Other AEDs were excluded because of their more toxic side effect profiles. A repeat EEG on 14 September 2001 was normal. She has not reported any side effects and has been seizure free since December 2000.

CASE 2

KC is a 6-year-old girl who presented in June 2000 with two episodes of twitching of the left face, arm, and leg accompanied by jabbery speech. Both episodes occurred during sleep. One month earlier her mother recalled an episode of drooling in bed.

The patient was a 7 lb 7 oz produce of a 37-week gestation born via scheduled Caesarean section because of prior Caesarean section. Developmental milestones were normal. She had no significant past medical history or family history of epilepsy. Neurologic exam was normal. An EEG on 28 June 2000 revealed bilateral centrotemporal spikes. Brain MRI was normal. The diagnosis of BECTS was made and the child was followed without treatment. However, over the next year, the seizures became more frequent and occurred as often as every other day. Levetiracetam was chosen for treatment because of its benign safety profile. Levetiracetam was initiated at 500 mg each evening at the beginning of June 2001. A repeat EEG on 15 June 2001 was normal. A third EEG on 7 December 2001 was also normal. The patient had one seizure in November 2001, characterised by left facial drooling. EEG at her follow-up visit on 7 October 2002 revealed frequent left centrotemporal spikes consistent with BRE. Her dose was increased to 750 mg each evening, and when the patient was seen on 5 September 2002, increased to 1000 mg each evening. She has had no drug related adverse effects or further seizures.

CASE 3

JA is a 10-year-old girl who had her first seizure while asleep in May 2000 and was subsequently diagnosed with BRE by another physician. The seizures were described as occurring within 2 hours of going to sleep, accompanied with facial twitching and progressing into bilateral tonic stiffening of the arms and legs. She was referred to us due to the refractory nature of these seizures, as she has four seizures in May 2002. Her past medical history, family history, neurological exam and MRI were negative. The EEG revealed right centrotemporal spikes. She began taking levetiracetam, reaching a final dose of 500 mg in the morning and 1000 mg in the evening over a 2-week interval. She remains seizure-free and reports no side effects.

DISCUSSION

The Food and Drug Administration approved levetiracetam in November 1999 as adjunctive treatment for partial onset seizures in adults based on three multicenter, randomised, double-blind, placebo-controlled clinical studies in patients with refractory partial seizures with or without secondary generalisation[12–14]. In addition, a safety, tolerability, and pharmacokinetic study of levetiracetam in 23 paediatric patients (ages 6–12 years) with partial onset seizures demonstrated that 12/23 (52%) had a $\geq$50% reduction in seizure frequency and 5/23 (22%) had a $\geq$75% improvement. Two patients (9%) were seizure free. The most common side effects were headache, infection, somnolence, anorexia, and nervousness[15]. Pharmacokinetic studies of these children revealed an increased clearance of levetiracetam (1.43 ± 0.36 ml/min/kg) compared to adults (1.13 ± 0.30 ml/min/kg), suggesting that children may require a higher daily maintenance dose than adults[16].

All three children in this series had recurrent seizures due to BECTS. After beginning levetiracetam, one child had one seizure; otherwise all the children were seizure free. Sedation was the only side effect, and this was mild, well tolerated, and transient. These encouraging results warrant consideration of levetiracetam for children with BECTS who require treatment. A formal clinical trial of levetiracetam in children with BECTS should be considered.

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